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TOBACCO INDUSTRY RESEARCH COMMITTEE
150 EAST FORTY SECOND STREET NEW YORK 17, N.Y.

Application For Research Grant

(Compare #89)
Activated Oct. 1, 1955
Renewed Aug. 1, 1956
Supplemented Oct. 1, '56
Present anniversary date
Aug. 31, 1957

Date:

July 22, 1957

1. Name of Investigator:

Dr. Caroline Bidell Thomas, M.D.

2. Title:

Associate Professor of Medicine

3. Institution

& Address:

The Johns Hopkins School of Medicine
710 North Washington Street
Baltimore 5, Maryland

4. Project or Subject:

Studies on Smoking in Healthy Young Adults.

5. Detailed Plan of Procedure (Use reverse side if additional space is needed):

It is proposed to study the effects of smoking, both acute and chronic, upon healthy young adults, to ascertain in what ways smokers as a group differ from nonsmokers, to observe the different individual circulatory reaction patterns appearing in a ballistocardiographic smoking test, and to attempt to modify those reaction patterns through the use of pharmacological substances in order to understand better the physiological mechanisms involved. The Johns Hopkins medical students are to be used as subjects for the smoking studies. The facilities and extensive data of the long-term study, in progress over ten years, of the precursors of hypertension and/or coronary heart disease supported by the National Heart Institute provide the basic materials needed. The large amount of work and money already invested in that study can be utilized effectively in obtaining answers to the question: Who is a smoker? Likewise, the follow-up program of the cardiovascular study, designed to determine just which subjects develop hypertension or coronary heart disease at an early age, will ultimately can make a valuable contribution to the smoking studies.

a. Comparison of smokers and nonsmokers among the Johns Hopkins medical students in regard to 1) family history of hypertension and/or coronary artery disease; 2) physiological characteristics; 3) psychological traits; and 4) educational, religious and family background.

During the past year many of these comparisons have been undertaken, and some of the statistical analyses are nearly complete (see Progress Note, Section I for Grant #89). However, much more remains to be done before these preliminary results are ready for publication. In some instances, it may prove desirable to add data now on hand from the classes of 1958, 1959 and 1960. Tabulations presented in the Progress Report are based on information from the classes of 1948 through 1957. More statistical computations need to be done on many aspects of the physiological and psychological

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studies, so far only touched upon. Finally, many portions of the data are awaiting analysis. These include:

- (1) Relationship of family history of obesity and diabetes to smoking habits of students.
- (2) Correlation of smoking habits with:
 - (a) health history of the students themselves.
 - (b) the effect of carotene-controlled anoxemia.
 - (c) the circulating eosinophil count as a measure of adrenal cortical activity.
 - (d) body build, using the ponderal index, height / $\sqrt{\text{weight}}$ as well as clinical observations.
 - (e) habits of sleeping, eating, drinking, self-medication, work, exercise and recreation.
 - (f) birthplace and ancestral background.
 - (g) educational background, including an analysis of whether the subjects attended private schools, boarding or day schools, religious affiliation and training.
 - (h)
 - (i)
 - (j) relationship of subject with father and mother and of parents with each other.
 - (k) factors leading to insecurity in childhood, including divorce of parents and death or chronic illness of a parent.

A good deal of mature consideration will be needed as to the best way to write up and publish this material in view of the current prominence given to research in regard to smoking by the popular press. Even though many of the preliminary findings described in the Progress Note are statistically significant, the numbers of subjects involved are not large, and we certainly want to avoid premature publicity.

(b) Ballistocardiographic studies of individual circulatory patterns of response to smoking.

During the past two years we have demonstrated the satisfactory reproducibility of the ballistocardiographic smoking test in a given individual. These studies have laid the ground work for those we are now undertaking; within the past few weeks, we have started on a new series of ballistocardiographic smoking studies designed to elucidate the differences in individual patterns of response to smoking. Through the use of various pharmacologic substances it is hoped that the roles played, in human beings, by the sympathetic nervous system, the adrenal gland and other physiologic mechanisms may be better understood. At present the effects of intravenous injections of small doses of hexamethonium are being compared with similar injections of normal salt solution. The same subjects are to have repeated tests, and the dosage is to be gradually increased with each test until a clear cut end point is obtained.

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Other substances under consideration for study include adrenalin, noradrenalin, Wyamin, atropine, cortisone, ACTH and alcohol. This approach is a difficult one, particularly when it is remembered that elevation of heart rate beyond a certain point makes it difficult or impossible to make accurate ballistocardiographic measurements of stroke volume. It is our intention to keep the dosages small and to search for leads which may open up new areas of study, at least in regard to some of the substances employed.

c. Studies using circulatory ballistocardiographic patterns as the basis for classification and comparison.

Now that over 300 subjects have had ballistocardiographic smoking tests, students can be classified in new ways according to their physiologic responses to smoking. Our first paper on the smoking test indicated that different degrees of increase or decrease in cardiac output after smoking a single cigarette were significantly linked with differences in heritage in regard to hypertension or coronary heart disease (1). Comparisons of the physiologic, metabolic and psychologic attributes of those who are hyperreactive or nonreactive to smoking may prove to be much more revealing than the comparisons of smokers with nonsmokers, particularly in regard to psychological differences.

d. Further studies of the relationship of smoking to cholesterol levels.

In view of the finding that smokers have higher average cholesterol levels than nonsmokers (see Progress Note Section I D), it may be possible during the coming year to throw more light on this problem by inducing a group of regular smokers to stop smoking and to observe their cholesterol levels weekly over the ensuing months.

Itemized Annual Budget

Salaries

Director, Dr. Caroline Bedall Thomas	\$2,000
Fellow, part-time, Dr. Edmund A. Murphy	1,000
Chief Statistical Clerk	2,800
Assistant Statistical Clerk	2,400
Student Assistants	600
	<hr/>
	8,800
	300
	<hr/>

Expendable Supplies	800
Permanent Equipment	300
Other: costs of tabulation and publication, cholesterol determinations for smoking studies, etc.	<hr/> 300
	\$ 9,400
	1,600
	<hr/>

Overhead (20%)	140
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	1280
	<hr/>

TOTAL

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Thomas, C. B., Bateman, J. L. and Lindberg, E. F., Ann. Int. Med. 44:874, 1956

6. Budget Plan:

Salaries	\$8,800.
Expendable Supplies	300.
Permanent Equipment	00.
Overhead	<i>15%</i>
Other	
Total	<i>11,200.</i> <i>1410 00</i>
	<i>\$11,200. 10810 00</i>

7. Anticipated Duration of Work: two years.

8. Facilities and Staff Available:

There is ample work space in conjunction with our major project including a separate laboratory equipped with Starr-type ballistocardiograph and a double-channel Sanborn Viso-cardiotte. Dr. Murphy, the part-time Fellow who has conducted the statistical studies of variability this year (see Progress Note Section II) is available and is well trained for the proposed studies. He has worked under Dr. John McMichael in England on the effect of hexamethonium in hypertensive patients. The entire project will be under my direct supervision, and will be assisted by the secretary and the physiological technician of the long-term project where required.

9. Additional Requirements:

Continuation of the advice and counsel of Miss Mary Burke, Statistician to the Tobacco Industry Research Committee.

10. Additional Information (Including relation of work to other projects and other sources of supply):

The aims of the project outlined above are in harmony with those of Grant H-1891 (C3) entitled "Precursors of Hypertension and Coronary Artery Disease" awarded by the National Heart Institute. The funds from that source do not include most of the items covered by the budget given above. Where similar items exist in each of the two budgets, it is because the budget from Grant H-1891 (C3) is insufficient to meet the total expense of a given item, and the two budgets will be used in such a way that they supplement each other.

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Signature

John E. Beall Thomas

Director of Project

/ / *Samuel P. Asper, Dean, by*
Business Officer of the InstitutionSamuel P. Asper, Jr.
Associate Dean